Glossary of Terms Used in Medicinal Chemistry
(IUPAC Recommendations 1998)

A to H

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Active transport*

Active transport is the carriage of a solute across a biological membrane from low to high concentration that requires the expenditure of (metabolic) energy.

Address-message concept

Address-message concept refers to compounds in which part of the molecule is required for binding (address) and part for the biological action (message).

ADME

Abbreviation for **Absorption, Distribution, Metabolism, Excretion.** (See also **Pharmacokinetics; Drug disposition)**.

Affinity

Affinity is the tendency of a molecule to associate with another. The **affinity** of a **drug** is its ability to bind to its biological target (**receptor**, **enzyme**, transport system, etc.) For pharmacological **receptors** it can be thought of as the frequency with which the **drug**, when brought into the proximity of a **receptor** by diffusion, will reside at a position of minimum free energy within the force field of that **receptor**.

For an **agonist** (or for an **antagonist**) the numerical representation of **affinity** is the reciprocal of the equilibrium dissociation constant of the ligand-**receptor** complex denoted K_A, calculated as the rate constant for offset (k_{-1}) divided by the rate constant for onset (k_1).

Agonist***

An **agonist** is an endogenous substance or a **drug** that can interact with a **receptor** and initiate a physiological or a pharmacological response characteristic of that **receptor** (contraction, relaxation, secretion, **enzyme** activation, etc.).

Allosteric binding sites

Allosteric binding sites are contained in many **enzymes** and **receptors**. As a consequence of the binding to **Allosteric binding sites**, the interaction with the normal ligand may be either enhanced or reduced.

Allosteric enzyme*

An **allosteric enzyme** is an **enzyme** that contains a region to which small, regulatory molecules ("effectors") may bind in addition to and separate from the substrate binding site and thereby affect the catalytic activity.

On binding the effector, the catalytic activity of the **enzyme** towards the substrate may be enhanced, in which case the effector is an activator, or reduced, in which case it is a de-activator or inhibitor.

Allosteric regulation

Allosteric regulation is the regulation of the activity of **allosteric enzymes**. (See also **Allosteric binding sites**; **Allosteric enzymes**).

Analog

An **analog** is a **drug** whose structure is related to that of another **drug** but whose chemical and biological properties may be quite different. (See also **Congener**).

Antagonist***

An **antagonist** is a **drug** or a compound that opposes the physiological effects of another. At the **receptor** level, it is a chemical entity that opposes the **receptor**-associated responses normally induced by another bioactive agent.

Antimetabolite***

An **antimetabolite** is a structural **analog** of an intermediate (substrate or **coenzyme**) in a physiologically

occurring metabolic pathway that acts by replacing the natural substrate thus blocking or diverting the biosynthesis of physiologically important substances.

Antisense molecule

An **antisense molecule** is an **oligonucleotide** or **analog** thereof that is complementary to a segment of RNA (ribonucleic acid) or DNA (deoxyribonucleic acid) and that binds to it and inhibits its normal function.

Autacoid

An **autacoid** is a biological substance secreted by various cells whose physiological activity is restricted to the vicinity of its release; it is often referred to as local **hormone**.

Autoreceptor

An **autoreceptor**, present at a nerve ending, is a **receptor** that regulates, via positive or negative feedback processes, the synthesis and/or release of its own physiological ligand. (See also **Heteroreceptor**).

Bioassay***

A **bioassay** is a procedure for determining the concentration, purity, and/or biological activity of a substance (e.g., vitamin, **hormone**, plant growth factor, antibiotic, **enzyme**) by measuring its effect on an organism, tissue, cell, **enzyme** or **receptor** preparation compared to a standard preparation.

Bioisostere

A **bioisostere** is a compound resulting from the exchange of an atom or of a group of atoms with another, broadly similar, atom or group of atoms. The objective of a bioisosteric replacement is to create a new compound with similar biological properties to the parent compound. The bioisosteric replacement may be physicochemically or topologically based. (See also **Isostere**)

Bioprecursor prodrug

A **bioprecursor prodrug** is a **prodrug** that does not imply the linkage to a carrier group, but results from a molecular modification of the active principle itself. This modification generates a new compound, able to be transformed metabolically or chemically, the resulting compound being the active principle.

Biotransformation

Biotransformation is the chemical conversion of substances by living organisms or **enzyme** preparations.

CADD

See **Computer-assisted drug design**.

Carrier-linked prodrug (Carrier prodrug)

A **carrier-linked prodrug** is a **prodrug** that contains a temporary linkage of a given active substance with a transient carrier group that produces improved physicochemical or pharmacokinetic properties and that can be easily removed *in vivo*, usually by a hydrolytic cleavage.

Cascade prodrug

A **cascade prodrug** is a **prodrug** for which the cleavage of the carrier group becomes effective only after unmasking an activating group.

Catabolism***

Catabolism consists of reactions involving endogenous organic substrates to provide chemically available energy (e.g., ATP) and/or to generate metabolic intermediates used in subsequent anabolic reactions.

Catabolite

A **catabolite** is a naturally occurring **metabolite**.

Clone*

A **clone** is a population of genetically identical cells produced from a common ancestor. Sometimes, "**clone**" is also used for a number of recombinant DNA (deoxyribonucleic acid) molecules all carrying the same inserted sequence.

Codon*

A **codon** is the sequence of three consecutive **nucleotides** that occurs in mRNA which directs the incorporation of a specific amino acid into a protein or represents the starting or termination signals of protein synthesis.

Coenzyme

A **coenzyme** is a dissociable, low-molecular weight, non-proteinaceous organic compound (often **nucleotide**) participating in enzymatic reactions as acceptor or donor of chemical groups or electrons.

Combinatorial synthesis

Combinatorial synthesis is a process to prepare large sets of organic compounds by combining sets of building blocks.

Combinatorial library

A **combinatorial library** is a set of compounds prepared by **combinatorial synthesis**.

CoMFA

See **Comparative Molecular Field Analysis**.

Comparative Molecular Field Analysis (CoMFA)**

Comparative molecular field analysis (CoMFA) is a **3D-QSAR** method that uses statistical correlation techniques for the analysis of the quantitative relationship between the biological activity of a set of compounds with a specified alignment, and their three-dimensional electronic and steric properties. Other properties such as hydrophobicity and hydrogen bonding can also be incorporated into the analysis. (See also **Three-dimensional Quantitative Structure-Activity Relationship [3D-QSAR]**).

Computational chemistry**

Computational chemistry is a discipline using mathematical methods for the calculation of molecular properties or for the simulation of molecular behaviour.

Computer-assisted drug design (CADD)**

Computer-assisted drug design involves all computer-assisted techniques used to discover, design and optimize biologically active compounds with a putative use as **drugs**.

Congener***

A **congener** is a substance literally *con-* (with) *generated* or synthesized by essentially the same synthetic chemical reactions and the same procedures. **Analogs** are substances that are analogous in some respect to the prototype agent in chemical structure.

Clearly **congeners** may be **analogs** or vice versa but not necessarily. The term **congener**, while most often a synonym for homologue, has become somewhat more diffuse in meaning so that the terms **congener** and **analog** are frequently used interchangeably in the literature.

Cooperativity

Cooperativity is the interaction process by which binding of a ligand to one site on a macromolecule (**enzyme**, **receptor**, etc.) influences binding at a second site, e.g. between the substrate binding sites of an **allosteric enzyme**. Cooperative **enzymes** typically display a sigmoid (S-shaped) plot of the reaction rate against substrate concentration. (See also **Allosteric binding sites**).

3D-QSAR

See **Three-dimensional Quantitative Structure-Activity Relationship**.

De novo* design*

***De novo* design** is the design of bioactive compounds by incremental construction of a ligand model within a model of the **receptor** or **enzyme** active site, the structure of which is known from X-ray or nuclear magnetic resonance (NMR) data.

Disposition

See **Drug disposition**.

Distomer

A **distomer** is the enantiomer of a chiral compound that is the less potent for a particular action. This definition does not excude the possibility of other effect or side effect of the **distomer** (See also **Eutomer**).

Docking studies

Docking studies are molecular modeling studies aiming at finding a proper fit between a ligand and its binding site.

Double-blind study

A ***double-blind study*** is a clinical study of potential and marketed **drugs**, where neither the investigators nor the subjects know which subjects will be treated with the active principle and which ones will receive a placebo.

Double prodrug (or pro-prodrug)

A **double prodrug** is a biologically inactive molecule which is transformed *in vivo* in two steps (enzymatically and/or chemically) to the active species.

Drug***

A **drug** is any substance presented for treating, curing or preventing disease in human beings or in animals. A **drug** may also be used for making a medical diagnosis or for restoring, correcting, or modifying physiological functions (e.g., the contraceptive pill).

Drug disposition

Drug disposition refers to all processes involved in the absorption, distribution **metabolism** and excretion of **drugs** in a living organism.

Drug latentiation

Drug latentiation is the chemical modification of a biologically active compound to form a new compound, which *in vivo* will liberate the parent compound. **Drug latentiation** is synonymous with **prodrug** design.

Drug targeting

Drug targeting is a strategy aiming at the delivery of a compound to a particular tissue of the body.

Dual action drug

A **dual action drug** is a compound which combines two desired different pharmacological actions at a similarly efficacious dose.

Efficacy

Efficacy describes the relative intensity with which **agonists** vary in the response they produce even

when they occupy the same number of **receptors** and with the same **affinity**. **Efficacy** *is not* synonymous to **Intrinsic activity**.

Efficacy is the property that enables **drugs** to produce responses. It is convenient to differentiate the properties of **drugs** into two groups, those which cause them to associate with the **receptors** (**affinity**) and those that produce stimulus (**Efficacy**). This term is often used to characterize the level of maximal responses induced by **agonists**. In fact, not all **agonists** of a **receptor** are capable of inducing identical levels of maximal responses. Maximal response depends on the efficiency of **receptor** coupling, i.e., from the cascade of events, which, from the binding of the **drug** to the **receptor**, leads to the observed biological effect.

Elimination

Elimination is the process achieving the reduction of of the concentration of a **xenobiotic** including its **metabolism**.

Enzyme*

An **enzyme** is a macromolecule, usually a protein, that functions as a (bio) catalyst by increasing the reaction rate.

In general, an **enzyme** catalyzes only one reaction type (reaction selectivity) and operates on only one type of substrate (substrate selectivity). Substrate molecules are transformed at the same site (regioselectivity) and only one or preferentially one of chiral a substrate or of a racemate is transformed (enantioselectivity[special form of stereoselectivity]).

Enzyme induction*

Enzyme induction is the process whereby an (inducible) **enzyme** is synthesized in response to a specific inducer molecule. The inducer molecule (often a substrate that needs the catalytic activity of the inducible **enzyme** for its **metabolism**) combines with a repressor and thereby prevents the blocking of an operator by the repressor leading to the translation of the gene for the **enzyme**.

Enzyme repression*

Enzyme repression is the mode by which the synthesis of an **enzyme** is prevented by repressor molecules.

In many cases, the end product of a synthesis chain (e.g., an amino acid) acts as a feed-back corepressor by combining with an intracellular aporepressor protein, so that this complex is able to block the function of an operator. As a result, the whole operation is prevented from being transcribed into mRNA, and the expression of all **enzymes** necessary for the synthesis of the end product **enzyme** is abolished.

Eudismic ratio

Eudismic ratio is the **potency** of the **eutomer** relative to that of the **distomer**.

Eutomer

The **Eutomer** is the enantiomer of a chiral compound that is the more potent for a particular action (See also **Distomer**).

Genome*

A **genome** is the complete set of chromosomal and extrachromosomal genes of an organism, a cell, an organelle or a virus; the complete DNA (deoxyribonucleic acid) component of an organism.

Hansch analysis**

Hansch analysis is the investigation of the quantitative relationship between the biological activity of a series of compounds and their physicochemical substituent or global parameters representing hydrophobic, electronic, steric and other effects using multiple regression correlation methodology.

Hapten***

A **hapten** is a low molecular weight molecule that contains an antigenic determinant but which is not itself antigenic unless combined with an antigenic carrier.

Hard drug

A **hard drug** is a nonmetabolizable compound, characterized either by high lipid solubility and accumulation in adipose tissues and organelles, or by high water solubility.

In the lay press the term "**Hard Drug**" refers to a powerful **drug** of abuse such as cocaine or heroin.

Heteroreceptor

A **heteroreceptor** is a **receptor** regulating the synthesis and/or the release of mediators other than its own ligand (See also **Autoreceptor**).

Homologue

The term **homologue** is used to describe a compound belonging to a series of compounds differing from each other by a repeating unit, such as a methylene group, a peptide residue, etc.

Hormone***

A **hormone** is a substance produced by endocrine glands, released in very low concentration into the bloodstream, and which exerts regulatory effects on specific organs or tissues distant from the site of secretion.

Hydrophilicity**

Hydrophilicity is the tendency of a molecule to be solvated by water.

Hydrophobicity**

Hydrophobicity is the association of non-polar groups or molecules in an aqueous environment which arises from the tendency of water to exclude non polar molecules. (See also **Lipophilicity**).

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